CLAIMS

We claim:

1. A method of identifying a gene involved in cell proliferation comprising the steps of:

(a) exposing a fish to a mutagen;

(b) mating said fish with a wild-type fish to produce an F1 generation;

(c) exposing the eggs of said F1 generation to inactivated fish sperm to create haploid embryos; and

(d) screening said haploid embryos for cell proliferation defects wherein an embryo with cell proliferation defects harbors a mutant gene involved in cell proliferation.

2. The method of claim 1, further comprising a steps of:

(e) mating the F1 generation with wild-type male fish to produce an F2 generation;

(f) raising said F2 generation to adulthood;

(g) mating a female member of the F2 generation with a male member of the F2 generation to produce F3 embryos;

(h) screening the F3 diploid embryos for cell proliferation defects wherein an embryo with cell proliferation defects harbors a mutant gene involved in cell proliferation.

3. The method of claim 1, wherein the fish in the step (a) is a male fish.

4. The method of claim 1 wherein the fish is a zebrafish.

5. The method of claim 1, wherein the mutagen is an alkylating agent.

6. The method of claim 1 selected from a group consisting of ENU and MNU.

7. The method of claim 1 or 2 further comprising a step of positional cloning of a nucleic acid sequence of the mutant gene.

8. The method of claim 1 or 2, wherein the screening is performed using an antibody against a cell cycle component.

9. The method of claim 8, wherein the antibody is specific for a protein selected from the croup consisting of phospho-histone H3, phosphorylated MAP kinase, phosphorylated MEK-1, BM28, cyclin E, p53, Rb and PCNA.

10. The method of claim 1 or 2, wherein the screening is performed using nucleic acids recognizing cell cycle components.

11. The method of claim 9, wherein the nucleic acid is PCNA or cyclin b-1.

12. The method of claim 1 or 2, wherein the screening is performed using flow cytometry.

13. The method of claim 1 or 2, wherein the screening is performed using apoptosis markers.

14. The method of claim 13, wherein the apoptosis marker is selected from the group consisting of Annexin V, TUNEL Stain, 7-amino-actinomycin D and Caspase substrates.

15. The method of claim 1 or 2, wherein the screening is preformed using BrdU staining.

16. The method of claim 1 or 2, wherein the screening is performed using an irradiation analysis.

17. The method of claim 1 or 2, further comprising a step of positional cloning of the gene involved in cell proliferation.

18. A method of identifying a gene involved in carcinogenesis comprising the steps of:

(a) exposing a fish to a mutagen;

(b) mating said fish with a wild-type fish to produce an F1 generation;

(c) exposing the eggs of said F1 generation to inactivated fish sperm to create haploid embryos; and

(d) screening said haploid embryos for cell proliferation defects wherein an embryo with cell proliferation defects harbors a mutant gene involved in cell proliferation;

(e) mating an F1 generation female of step (c) harboring a mutant gene involved in cell proliferation as determined in step (d) with a wild-type fish to produce an F2 generation;

(f) exposing a wild-type fish and a member of the F2 generation to a carcinogen; and

(g) comparing the tumor formation in the wild-type and the member of the F2 generation fish wherein an accelerated tumor formation in the F2 generation fish indicates a gene involved in carcinogenesis.

19. The method of claim 18, wherein the fish is a zebrafish.

20. The method of claim 18, further comprising a step of positional cloning of the gene involved in carcinogenesis.

21. The method of claim 18, wherein the screening is performed using an antibody against a cell cycle component.

22. The method of claim 21, wherein the antibody is specific for a protein selected from the croup consisting of phospho-histone H3, phosphorylated MAP kinase, phosphorylated MEK-1, BM28, cyclin E, p53, Rb and PCNA.

23. The method of claim 18, wherein the screening is performed using nucleic acids recognizing cell cycle components.

24. The method of claim 23, wherein the nucleic acid is PCNA or cyclin b-1.

25. The method of claim 18, wherein the screening is performed using flow cytometry.

26. The method of claim 18, wherein the screening is performed using apoptosis markers.

27. The method of claim 26, wherein the apoptosis marker is selected from the group consisting of Annexin V, TUNEL Stain, 7-amino-actinomycin D and Caspase substrates.

28. The method of claim 18, wherein the screening is preformed using BrdU staining.

29. The method of claim 18, wherein the screening is performed using an irradiation analysis.